CLAIMS

1. An oral vaccine comprising a nucleic acid operatively encoding an antigen complexed with or entrapped within liposomes formed from liposome forming components including

a) at least one cationic compound having the general formula I,

$$R^1OCH_2CH(OR^2)CH_2R^5X^1R^6{}_n \qquad I$$

in which R^1 and R^2 are the same or different and are selected from groups of the formula $CH_3(CH_2)_a(CH{=}CH\text{-}CH_2)_b(CH_2)_c(CO)_d$-

in which b is 0 to 6, a and c are each selected from 0-23 and (a + c + 3b) is in the range 12-23 and d is 0 or 1;

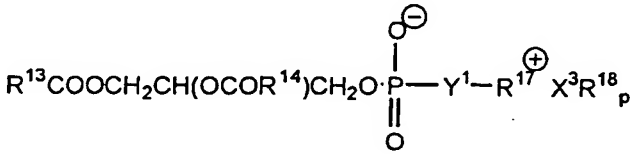
R^5 is a bond or a C_{1-8} alkanediyl group;

X^1 is N, P or S;

n is 3 where X^1 is N or P and is 2 where X^1 is S; and

the groups R^6 are the same or different and are selected from hydrogen, C_{1-8} alkyl, C_{6-12} aryl or aralkyl, or two or three of the groups R^6 together with X^1 may form a saturated or unsaturated heterocyclic group having 5 to 7 ring atoms;

b) at least one zwitteronic phospholipid having the general formula II



III

in which R^3 and R^4 are the same or different and are selected from groups of the formula $CH_3(CH_2)_e(CH{=}CH\text{-}CH_2)_f(CH_2)_g$-

in which f is 0 to 6, each of e and g are 0 to 23 and e + g + 3f is in the range 12 to 23;

R^7 is a C_{1-8} alkanediyl group;

Y is -O- or a bond;

X^2 is N, P or S;

m is 3 when X^2 is N or P and is 2 when X^2 is S; and

the groups R^8 are the same or different and are selected from the group consisting of hydrogen, C_{1-8} alkyl, C_{6-11} aryl or aralkyl, or two or three of the groups R^8 together with X^3 may form a saturated or unsaturated heterocyclic group having 5 to 7 ring atoms;

provided that in at least one of the groups R^1, R^2, R^3 and R^4, b or f, as the case may be, is 0.

2. A vaccine according to claim 1 in which $R^1=R^2$ and $R^3=R^4$.

3. A vaccine according to claim 2 in which R^1 and R^2 represent a different group to R^3 and R^4.

4. A vaccine according to claim 2 and claim 3 in which in R^1 and R^2 b=1 and in which (a + c) is in the range 10-20.

5. A vaccine according to any of claims 2 to 4 in which d = 0.

6. A vaccine according to any of claims 2 to 5 in which f = 0.

7. A vaccine according to any preceding claim in which X^1 is N and in which the R^6 groups are all C_{1-4} alkyl.

8. A vaccine according to any preceding claim which comprises two zwitterionic phospholipids each having the formula II, in which Y is O, and X^2 is N, and the groups R^8 of the first phospholipid are all hydrogen and the groups R^8 of the second phospholipid and all C_{1-4} alkyl, preferably methyl.

9. A vaccine according to claim 8 in which, in each phospholipid Y is O and R^7 is $(CH_2)_h$ in which h is 2 or 3.

10. A vaccine according to claim 8 or claim 9 in which the groups R^3 and R^4 of the first phospholipid are the same and each is a group in which f=1 and (e + g) is in the range 10 to 20, preferably 12 to 14.

11. A vaccine according to any of claims 8 to 10 in which the groups R^3 and R^4 of the second phospholipid are the same and each is a group in which f=0 and e + g is in the range 15 to 23, preferably 15-17.

12. An oral vaccine comprising a nucleic acid encoding an antigen complexed to or entrapped within liposomes formed from liposome forming components including at least one glycerolipid, at least one cationic

compound and at least one zwitterionic phospholipid characterised in that at least one glycerolipid is an O'O-dialkanoyl or O,O'-dialkyl phospholipid.

13. A vaccine according to claim 12 in which the glycerolipid is a compound of the general formula II defined in claim 1 in which f is 0 in both R^3 and R^4.

14. An oral vaccine comprising a nucleic acid encoding an antigen complexed to and/or entrapped within liposomes formed from liposome forming components including at least one cationic compound and at least one zwitterionic phospholipid characterised in that the liposome forming components include at least 25 mole%, preferably at least 50 mole%, of components which individually have a transition temperature of more than 40°C.

15. A vaccine according to any of claims 12 to 14 in which the zwitterionic phospholipid is selected from the group consisting of distearoylphosphatidylcholine, distearoylphosphatidylethanolamine, diplamitoylphosphatidylcholine, dipalmitoylphosphatidylethanolamine and mixtures thereof.

16. A vaccine according to any of claims 12 to 15 in which the cationic compound is a compound of the general formula I as defined in claim 1.

17. A vaccine according to any of claims 12 to 15 in which the cationic compound is DC-cholesterol.

18. A method in which a human or a non-human animal is vaccinated by administering a vaccine according to any preceding claim orally whereby an immune response to the encoded antigen is generated.

19. A method of entrapping polynucleotide into liposomes involving the steps of:

i) forming an aqueous suspension comprising naked polynucleotide, which operatively encodes an immunogenic polypeptide useful to induce a desired immune response in a human or animal subject, and preformed liposomes formed of

liposome forming components as defined in claim 1, claim 12 or claim 14,

ii) freeze-drying or spray-drying the suspension, and

iii) rehydrating the product of step ii) to form dehydration/rehydration vesicles.

20. A method according to claim 19 comprising the further steps of:

iv) subjecting the aqueous suspension of dehydration/rehydration vesicles from step iii to microfluidization to control their size; and

v) optionally separating non entrapped polynucleotide from liposomes.